



**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
(PCT Article 36 and Rule 70)

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| Applicant's or agent's file reference<br>100884-1 WO  | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)   |  |
| International application No.<br>PCT/SE 03/01706  | International filing date (day/month/year)<br>05.11.2003   | Priority date (day/month/year)<br>07.11.2002 |
| International Patent Classification (IPC) or both national classification and IPC<br>C07D295/155  |  |  |
| Applicant<br>ASTRAZENECA AB et al.  |  |  |
| <p>1. This International preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>   |  |  |
| <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input checked="" type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p> |  |  |
| Date of submission of the demand<br><br>14.05.2004  | Date of completion of this report<br><br>22.03.2005  |  |
| Name and mailing address of the international preliminary examining authority:<br><br> European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465   | Authorized Officer<br><br>Cortés, J<br><br>Telephone No. +49 89 2399-8206<br><br> |  |

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EXAMINATION REPORT**

International application No. **PCT/SE 03/01706**

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-108 as originally filed

**Claims, Numbers**

1-21 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

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**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious); or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 14-16

because:

☒ the said international application, or the said claims Nos. 14-16 relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

|                               |             |             |
|-------------------------------|-------------|-------------|
| Novelty (N)                   | Yes: Claims | 1-21        |
|                               | No: Claims  |             |
| Inventive step (IS)           | Yes: Claims |             |
|                               | No: Claims  | 1-21        |
| Industrial applicability (IA) | Yes: Claims | 1-13, 17-21 |
|                               | No: Claims  |             |

2. Citations and explanations

**see separate sheet**

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**VI. Certain documents cited**

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

**Re Item III****Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 14-16 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims (Article 34(4)(a)(i) PCT).

**Re Item V****Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

The following documents have been cited in the International Search Report:

D1: WO 93 15062 A1

D2: PLOBECK NIKLAS ET AL.: 'New diarylmethylpiperazines as potent and selective nonpeptidic delta opioid receptor agonists with increased in vitro metabolic stability', J. MED. CHEM., vol. 43, 2000, pages 3878 - 3894, XP002973657

**Novelty (Article 33(2) PCT)**

The present compounds are a new selection of the compounds in D1. They differ from the structurally closest related examples 32 and 33 in that the piperazine is unsubstituted in positions 2,3,5 and 6.

The process of claim 18 differs from the process in D2 (scheme 9) in the nitro substituent of the final product.

The present claim set is therefore novel.

**Inventive Step (Article 33(3) PCT)**

D1 generically discloses the present compounds as well as their medical use. D1 can be regarded as the closest prior art.

The problem of the invention was the provision of new compounds for the treatment of

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pain or gastrointestinal disorders.

Since the present compounds as well as their medical use have been generically disclosed in D1 the present application lacks an inventive step.

**Re Item VI**

**Certain documents cited**

Reference is made to the following P-documents:

D3: WO 02 094794 A1

The priority documents pertaining to the present application were not available at the time of establishing this report. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the P-document cited in the international search report could become relevant to assess whether the present claims satisfy the criteria set forth in Article 33(1) PCT.